

AMENDMENTS TO THE SPECIFICATION:

Please amend the indicated paragraphs of the specification in accordance with the amendments indicated below.

Page 1: First full paragraph, amend the title as indicated below:

A ~~NOVEL~~ METHOD FOR PREDICTING THE SPATIAL-ARRANGEMENT
TOPOLOGY OF AN AMINO ACID SEQUENCE USING FREE ENERGY
COMBINED WITH SECONDARY STRUCTURAL INFORMATION

Pages 7-9: Paragraph bridging pages 7-8, amend as indicated below:

Further, the invention of this application may comprise the following
steps: ~~inputting an amino acid sequence of a protein,~~

- A. inputting an amino acid sequence of a protein,
- B. preparing information on the secondary structure of the said amino acid sequence by way of at least one theoretical or experimental estimate,
- C. applying the CLE method to the said amino acid sequence and secondary structure information to evaluate the free energy of a combinatorial number of β -strand and α -helix arrangements as rapidly as polynomial time: $c(n-1)(n+1)$ wherein c is a constant and n is the number of secondary structure elements found in the said amino acid in ~~2A~~ A and prepared in B ~~2B~~,
- D. applying the CLE method in conjunction with other thermodynamic potentials that approximate hydrophobic,

electrostatic and polar interactions, but not limited to these aforementioned thermodynamic potentials stated herein, in a thermodynamic calculation to account for both short and long range folding interactions and predict a minimum free energy and corresponding topology of the said amino acid sequence,

- E. applying the CLE method to predict the global folding kinetics of the said amino acid sequence, and
- F. storing the information in a data file or in other form of digital memory.

Pages 11-12: Paragraph bridging pages 11-12, amend as indicated below:

Here, the total CLE contribution to the free energy (ΔG_{cle}) can be calculated by equation (2):

$$\Delta G_{cle} = \Delta G_{\xi}^o + \sum_{all_bonds(i,j)} \Delta G_{ij} + \sum_{i',j'} f_{i'j'}(\xi) \quad (2)$$

wherein, ΔG_{ij} is defined in equation (1), i' and j' are indices specifying two secondary structure elements (α -helices or β -strands) that are joined together by the corresponding set of bonds i and j , $f_{i'j'}(\xi)$ is a positive definite penalty function used to enforce topology constraints on the minimum allowed sequence length of a loop connecting two elements of secondary structure $i' j'$ and is a function of the persistence length ξ , and ΔG_{ξ}^o is a renormalization correction and is an integral function of ξ as shown by equation (3):

$$\Delta G_{\xi}^o = \frac{(\gamma + 1/2)Nk_B T}{D\xi} \int_1^{\xi} \left(\frac{\ln(x)}{(1-x)} + 1 \right) dx \quad (3)$$

wherein, ξ , γ , k_B , and T mean the same as defined in the disclosure claim 7, N indicates the number of amino acids in the said sequence, D is the dimensionality of the system, the limits in the integral ($1 \rightarrow \xi$) indicate the change in the number of degrees of freedom from an individual amino acid residue to a cluster of ξ amino acids treated as a group (where $\xi > 1$ amino acid and ξ need not be an integer) and x is dummy variable in the integral substituting for ξ .